

(74)

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(54)

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3

(dendritic material)

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가

PCT/AU95/00350(WO 95/34595)

PCT/AU97/00447(WO 98/03573)

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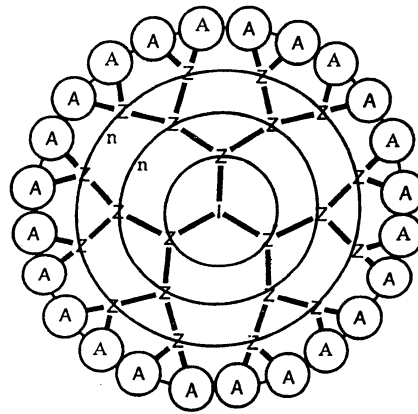
가

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n (generation)

A

X

Z

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(I),

가

PAMAM), 4,507,466, 4,289,872, 4,558,120, 4,410,688 (4,568,737, 4,587,329 (

4,289,872 4,410,688

가

WO 88/01178, WO 88/01179 WO 88/01180

가

WO 9

5/24221

(director)

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88/01179 WO 88/01180

WO 88/01178, WO

2

(PAMAM) 가, 2 PAMAM(EDA)

() (PPI)

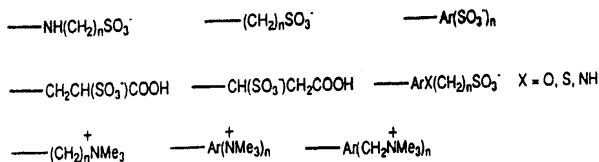
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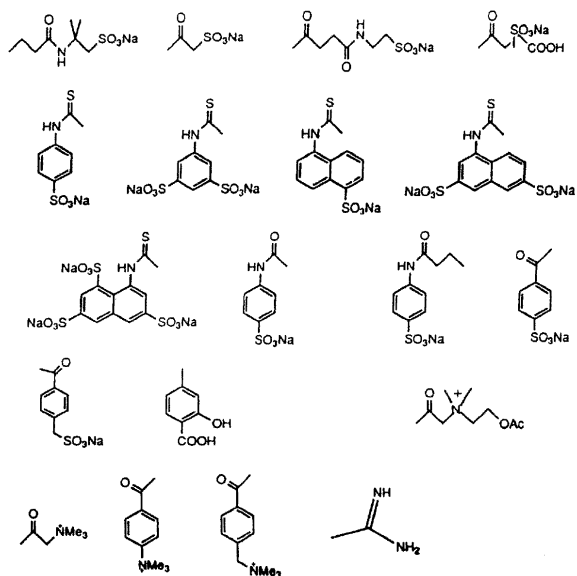
가 OH, SH

가

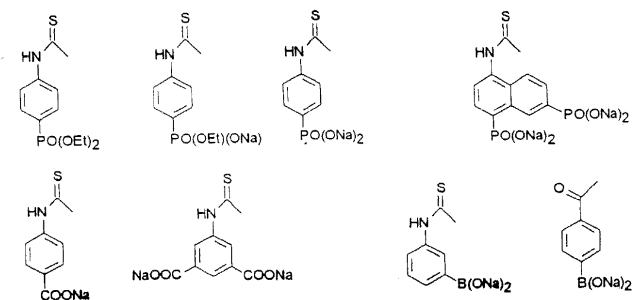
(), 1, 2, 3, 4

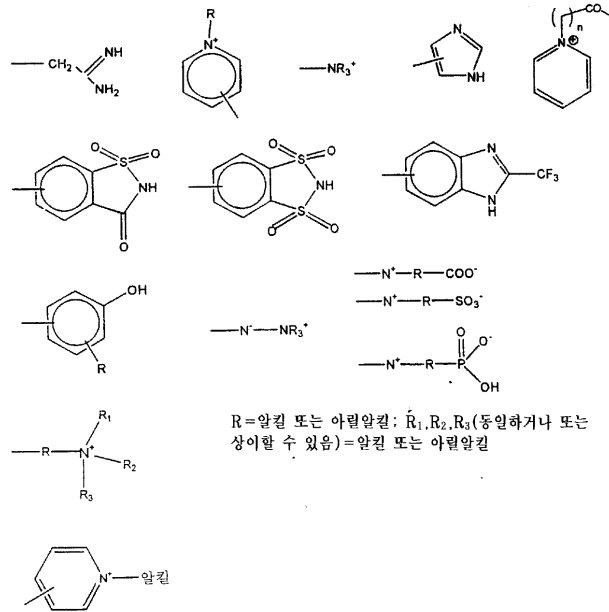
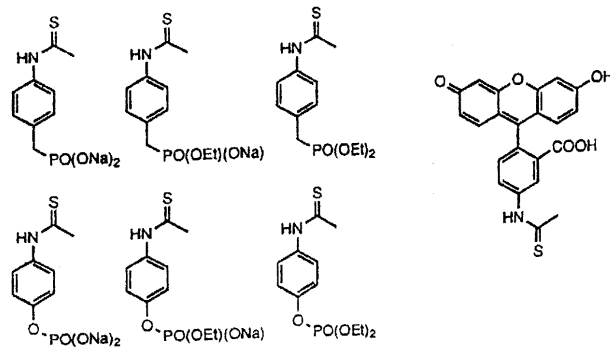
0, n 0 1 20) (n





—ArXP(=O)(OR)₂ X=O, CH₂, CHF, CF₂ R=알킬, 아릴, H, Na
 —ArXP(=O)(OR¹)(NR²R³) X=O, CH₂, CHF, CF₂ R¹=알킬, 아릴, H, Na R², R³=알킬, 아릴
 —Ar[P(=O)(OR)₂]_n R=알킬, 아릴, H, Na n=1-3
 —Ar[B(OH)₂]_n n=1-3 —Ar[COOH]_n n=1-3





O- N- O- N- N- O- N-
 4 가 2-, 7-, 9- 5-NAc 가

1, n 1 20, 1 10
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A () ()
 -CH₂ -, -CH="CH-", -C C-, -O- -S-, m 1 15
 -(CH₂)_m - Z - (CH₂)_m - () , Z

(,) 가 가 , ,
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 (,)

(a) , (b) 가
 , ,
 (, ,)
 가 , ,

1 kg 1 (0.01 1 mg) , 1 kg 0.01 mg 1000 mg/kg 가 (

- (a) (, (,) , (d) :
- (b) (, ,) , ()
- (c) (, ,) ,

(d) (, ,).

1 4 HIV Vpr P3 BRI 29237
 , PAMAM 4,507,466 , 4,558,120 , 4,568,737 4,587,329
 , PAMAM(EDA)
 , BHAlys_x lys_y lys_z 4,289,
 872 4,410,668
 PAMAM 1.0, PAMAM 2.0, PAMAM 3.0, PAMAM 4.0 PAMAM
 5.0 , PAMAM 4.0(EDA), BHAlyslys₂ , BHAlyslys₂ lys₄ , BHAlyslys₂
 lys₄ lys₈ , BHAlyslys₂ lys₄ lys₈ lys₁₆ , BHAlyslys₂ lys₄ lys₈ lys₁₆ lys₃₂ , BHAlyslys₂ lys₄ lys₈ lys₁₆ lys₃₂ lys₆₄
 4,289,872 , 4,410,688 , 4,507,466 , 4,558,120,
 4,568,737 4,578,239 WO 88/01178, WO 88/01179, WO 88/01180 WO 95
 /24221

1

2 - -2 -

APAMAM 1.0

(0.13 g, 1.0 mmol) 2 - -2 - (0.41 g, 2.0 mmol) (3 ml)
 가 . pH 8.0 . PAMAM 1.0(0.12 g, 0.33 mmol)
 (1 ml) 가 , 40% 4 가 .
 60 3 가 (Sephadex G10,)
 PAMAM 1.0 (0.51 g) . ¹H ¹³C nmr
 PAMAM 1.0 (70:30) . ¹³C nmr(D₂O): 31.0, 31.1,
 37.1, 37.7, 41.3, 48.6, 51.5, 53.1, 53.4, 55.6, 56.2, 61.2, 61.5, 178.3, 179.0, 179.8.

BPAMAM 2.0

PAMAM 2.0 2 - -2 - .
 (Sephadex G10,) . ¹H ¹³C nmr
 , PAMAM 2.0 (65:35) . ¹³C nmr(D₂O): 31.0, 3
 1.1, 37.1, 37.7, 41.3, 48.7, 51.5, 53.4, 55.6, 56.2, 61.2, 61.5, 178.4, 179.0, 179.1, 179.6.

CPAMAM 3.0BRI2783

PAMAM

3.0 2- -2- .¹H ¹³C nmr ,
 PAMAM 3.0 (50:50) .¹³C nmr(D₂O): 31.0, 31.1, 36.9, 37.4, 41.1,
 48.6, 51.5, 53.4, 55.7, 56.2, 61.1, 61.5, 178.2, 178.9, 179.0, 179.8.

DPAMAM 4.0BRI2784

PAMAM 3.0 PAMAM 4.0 2- -2- .¹H
¹³C nmr , PAMAM 4.0 (35:65) .¹
³C nmr(D₂O): 31.0, 31.1, 36.9, 37.3, 41.1, 48.5, 51.5, 53.5, 55.7, 56.2, 61.1, 61.5, 178.1, 178.9, 179.0,
 179.8.

2

APAMAM 1.0

4- (0.40 g, 1.5 mmol) DMF(1 ml) PAMAM 1.0(0.18 g, 0.5 mmol)
 DMF(3 ml) 가 . 20 ,
 (30 /0.1 mmHg)
 (2)
 (35 /25 mmHg) PAMAM 1.0 (0.36 g, 100%) .¹³C n
 mr(D₂O): 32.8, 33.3, 43.0, 43.5, 54.4, 174.5, 176.4.

(0.2 g, 1.6 mmol) (1 ml) PAMAM 1.0 (0.36 g, 0.5
 mmol) (5 ml) 가 11 .
 (0.60 g) .¹³C nmr(D₂O): 34.4, 43.1, 43.4, 54.0, 61.7, 171.3, 177.2.

1

가

BPAMAM 2.0

1:

4- (0.18 g, 0.07 mmol) DMF(1 ml) PAMAM 2.0(0.10 g, 0.1 mmol)
 DMF(3 ml) 가 . 20 ,
 (150 ml) 가 (3)
 (0.1 g, 0.8 mmol) (1 ml)
 가 , 3 ,
 (Sephadex LH 20,) PAMAM 2.0 (103 mg) .¹³C
 nmr(D₂O): 33.0, 35.7, 36.0, 37.7, 40.3, 43.0, 43.2, 53.4, 53.7, 56.0, 61.6, 171.2, 174.6, 178.5.

2:

(67 mg, 0.33 mmol) PAMAM 2.0, (52 mg, 0.05 mmol) DMF(2 ml) 가 2 (30 /10⁻³ mmHg) (117 mg) .¹
¹H ¹³C nmr (Sephadex G10,) N- PAMAM 2.0 (29 mg)
¹³C nmr(D₂O): 34.0, 34.2, 37.3, 43.0, 43.1, 43.3, 53.5, 54.0, 56.3, 175.4, 177.2, 177.5.

40% (7 ml) (1.6 mmol) (2 ml) 가 0 1 , 20 , 30 .
 가 , pH 9.0 , Sephadex G10 (20 mg) 1
¹³C nmr(D₂O): 33.0, 38.7, 42.9, 43.0, 43.1, 53.9, 54.3, 56.5, 61.6, 171.2, 176.4, 177.0.

3

APAMAM 1.0

(0.11 g, 1.1 mmol) PAMAM 1.0(0.12 g, 0.33 mmol) DMF(3 ml) 가
 (30 /10⁻⁴ mmHg) .¹H ¹³C nmr(D₂O)
 PAMAM 1.0 .¹³C nmr(D₂O): 33.1, 42.8, 43.1, 54.3, 135.0, 137.1, 169.1, 171.9, 173.3.

(4 ml) , (0.20 g, 1.6 mmol) 가 .
 4 .¹H ¹³C nmr(D₂O)
 PAMAM 1.0 1:1 .
 (Sephadex G10,) PAMAM 1.0 (107 mg) .¹³
¹³C nmr(D₂O): 33.3, 39.6, 40.0, 42.9, 43.1, 54.0, 67.9, 69.4, 173.8, 176.3, 177.6, 181.8.

BPAMAM 2.0

PAMAM 2.0 .¹³C nmr
 (D₂O): 32.8, 33.0, 38.7, 42.9, 53.8, 54.3, 56.5, 135.2, 136.8, 169.2, 171.9, 173.5, 174.6. ¹³C nmr PAMAM 2.0 (D₂O): 37.0, 40.1, 41.1, 43.0, 43.2, 43.9, 53.0, 53.3, 55.5, 68.0, 69.4, 173.8, 177.6, 179.1, 179.5, 179.8, 182.3.

CPAMAM 4.0BRI6038

(60 mg, 0.6 mmol) PAMAM 4.0(51 mg, 0.01 mmol) DMF(2 ml) 가
 (35 /10⁻⁴ mmHg) .¹H ¹³C nmr(D₂O) , PAMAM 4.0
 (2 ml) , (126
 mg, 1.0 mmol) (2 ml) 가 2 , .¹H ¹³
 C nmr(D₂O) PAMAM 4.0
 (Sephadex LH20,) , 24
 PAMAM 4.0 (90 mg) .¹H nmr(D₂O): 2.4 2.6, 2.7 3.1, 3.2 3.
 4, 3.9 4.0. ¹³C nmr(D₂O): 36.2, 39.8, 40.5, 43.0, 43.2, 53.5, 55.8, 68.1, 69.5, 173.8, 177.4, 177.6, 17
 8.7, 182.3.

4

N - (2 -)

a. N - (2 -)

(0.5 g, 5.0 mmol) 2 - (1.83 g, 5.0 mmol)
 (30 ml) 가 . (2.41 g) .¹³C nmr , 가
 N - (2 -) (1.762 g, 76%, mp 125
 127) .¹H nmr(CDCl₃): 0.86(t,12H,4xCH₃), 1.28(m,8H,4xCH₂), 1.50(m,8H,4xCH₂), 2.33(m,2
 H,CH₂COOH), 2.44(m,2H,CH₂CONH), 2.76(m,2H,CH₂NHCO),3.12(m,8H,4xCH₂N), 3.50(m,2H,CH₂SO₃⁻),
 7.53(br t,1H,NH). ¹³C nmr(CDCl₃): 13.5, 19.5, 23.8, 30.1, 30.9, 35.6, 50.0, 58.5, 172.0, 174.1.

b. 4 - N - (2 -)

(45 mg, 0.22 mmol) (1 ml) N - (2 -
) (94 mg, 0.20 mmol) (2 ml) 가 , .

A. N - (2 -) PAMAM

PAMAM 4.0BRI2786

4 - N - (2 -) (0.30 mmol) DMF(1 ml) , 5
 0% DMF(3 ml) PAMAM 4.0(51.5 mg, 0.01 mmol) 가
 (35 /10⁻⁵ mmHg)
 (2) , (134 mg)
 () IR 120(Na) 85 mg
 (Sephadex LH20,) N - (2 -) PAMA
 M 4.0 (45 mg) .¹³C nmr (D₂O): 33.2, 33.6, 35.5, 39.0, 39.5, 42.8, 43.2, 53.8, 54.1, 54.
 4, 56.6, 176.5, 176.9, 177.2, 178.9, 179.4.

N - (2 -)

PAMAM 1.0 PAMAM 3.0(BRI2785)

¹³C nmr PAMAM 3.0 (D₂O): 33.4, 35.5, 39.0, 39.5, 42.9, 43.2, 53.8, 54.1, 54.3, 56.5, 176.4, 176.
 9, 177.4, 178.9, 179.4.

^{13}C nmr PAMAM 1.0 (D_2O): 34.9, 35.5, 39.5, 42.9, 43.1, 53.7, 54.1, 179.0, 179.1, 179.3.

B N - (2 -)

BHAllyslys₂lys₄lys₈lys₁₆ BRI2789

(1 ml) BHAllyslys₂lys₄lys₈DBL₁₆ (36.5 mg, 5.0 μmol) (1 ml)
 가 2 , DMSO(2 ml)
 pH 8.5 4 - N - (2 -)
 (0.2 mmol) DMSO(1 ml) 가 ()
 50 /10⁻⁵ mmHg) (3)
 (99 mg) IR 120(Na)
 81 mg (Sephadex LH20,)
 N - (2 -) BHAllyslys₂lys₄lys₈lys₁₆ (39 mg) ^{13}C nm
 r(D_2O): 27.0, 32.3, 35.2, 35.3, 35.6, 35.7, 39.5, 43.5, 54.1, 58.5, 131.5, 132.0, 133.3, 145.1, 177.8, 1
 78.0, 178.4, 178.8, 178.9, 179.2, 179.7, 179.8.

N - (2 -) BHAllyslys₂, BHAllyslys₂lys₄ (BRI2787) BHAlly
 slys₂lys₄lys₈ (BRI2788)

^{13}C nmr BHAllyslys₂lys₄lys₈ (D_2O): 26.9, 32.3, 35.1, 35.3, 35.6, 35.7, 39.5, 43.5, 54.1, 58.5, 13
 1.6, 131.9, 132.2, 132.3, 133.2, 133.3, 145.0, 145.2, 177.2, 177.8, 177.9, 178.0, 178.2, 178.3, 178.6, 17
 8.7, 178.8, 178.9, 179.2, 179.3, 179.7, 179.8.

^{13}C nmr BHAllyslys₂lys₄ (D_2O): 26.9, 32.3, 35.1, 35.4, 35.7, 35.8, 39.5, 43.5, 54.1, 58.5, 61.8,
 131.7, 132.0, 132.2, 132.3, 133.2, 133.3, 145.0, 145.1, 177.3, 178.0, 178.3, 178.4, 178.7, 178.9, 179.0,
 179.3, 179.7, 179.8.

^{13}C nmr BHAllyslys₂ (D_2O): 26.9, 27.1, 32.2, 32.3, 34.7, 34.8, 35.1, 35.3, 35.6, 35.7, 39.5, 43.4,
 54.1, 58.6, 61.8, 131.7, 131.9, 132.2, 132.3, 133.3, 144.9, 145.0, 177.7, 178.4, 178.8, 179.0, 179.3, 180.
 0.

5

4 -

APAMAM 4.0BRI2791

4 - 1 (500 mg, 1.96 mmol) PAMAM 4.0(300 mg, 0.0582 mmo
 l) (10 ml) 가 53 2 가
 (Sephadex LH20,)
 4 - PAMAM 4.0 (370 mg)
 ^1H nmr (D_2O): 2.28, 2.52, 2.69, 3.15, 3.27, 3.60, 7.32(d,J="9Hz)," 7.72(d,J="9Hz)." ^{13}C nmr (D_2O):
 36.9, 41.1, 43.1, 48.3, 53.6, 55.8, 129.0, 131.1, 144.4, 178.5, 179.1, 184.4.

3 , 6 , 12 48 4 - PAMAM 1.0, PAMAM 2.0(BR
 I2790), PAMAM 3.0 PAMAM 5.0(BRI2991)

BPAMAM 4.0(EDA)BRI6045

4 - 1 (130 mg, 0.5 mmol) PAMAM 4.0(EDA) (69 mg, 0.01 mmol)
 (4 ml) 가 53 2 가
 (Sephadex LH20,)
 , 32 4 - PAMAM 4.0 (136 mg)
¹H nmr (D₂O): 2.30, 2.50, 2.70, 3.18, 3.62, 7.35(d,J="9Hz)," 7.72(d,J="9Hz)." ¹³C nmr (D₂O): 36.8, 41.0, 43.1, 48.4, 53.6, 55.7, 55.7, 128.9, 131.0, 144.3, 178.5, 179.0, 184.5.

C.BHAllyslys₂lys₄lys₈lys₁₆ BRI2792

(4 ml) BHAllyslys₂lys₄lys₈DBL₁₆ (0.73 g, 0.1 mmol) ()
 4 ml) 가 가 2
 (5 ml) IRA - 401(OH) , BHA
 lyslys₂lys₄lys₈lys₁₆ (0.49 g) (5 ml) , N,N - -
 N - (pH 9.5, 3 ml) 가 4 - 1 (1.30 g,
 5.1 mmol) 가 53 2 가 ,
 (Sephadex LH20,) IR 1
 20(Na) 4 - BHAllyslys₂lys₄lys₈lys₁₆
 (374 mg) . ¹H nmr(D₂O): 1.40,1.72, 3.08, 3.42, 4.24, 4.60, 7.30, 7.40(
 d,J="9Hz)," 7.78(d,J="9Hz)." ¹³C nmr (D₂O): 27.3, 32.5, 35.9, 43.7, 48.9, 58.6, 63.3, 128.8, 131.0, 14
 3.7, 144.7, 145.1, 177.7, 178.1, 183.8, 185.2.

16 , 64 128 4 - BHAllyslys₂lys₄lys₈ , BHAllyslys
₂lys₄lys₈lys₁₆lys₃₂ (BRI2992) BHAllyslys₂lys₄lys₈lys₁₆lys₃₂lys₆₄ (BRI2993)

6

3,6 -

APAMAM 4.0BRI2928

3,6 - (160 mg, 0.41 mmol) PAMAM 4.0(51 mg, 0.01 mmol) (3 m
 l) 가 53 2 가 ,
 (Sephadex LH20,)
 3,6 - PAMAM 4.0 (73 mg) . ¹H nmr(D₂O):
 2.30, 2.60, 2.74, 3.20, 3.57, 7.75, 7.86, 8.28. ¹³C nmr (D₂O): 35.0, 39.9, 43.1, 48.1, 53.8, 56.1, 128.4,
 128.6, 129.3, 131.0, 131.3, 136.0, 136.8, 138.2, 145.5, 146.0, 177.2, 177.8, 185.5.

3,6 -

PAMAM 2.0

B.PAMAM 4.0(EDA)BRI6046

3,6 - (220 mg, 0.57 mmol) PAMAM 4.0(EDA) (74 mg, 0.01 mmol)
 ol) (4 ml) 가 53 2 가 ,
 (Sephadex LH20,)
 , 32 3,6 - PAMAM 4.0 (148 mg)
¹H nmr(D₂O): 2.30, 2.80, 3.20, 3.54, 7.74, 7.85, 8.25. ¹³C nmr (D₂O): 36.0, 40.8, 43.1, 48.3,
 53.6, 55.9, 128.5, 129.4, 131.0, 131.3, 136.0, 136.8, 138.3, 145.5, 146.0, 178.2, 185.6.

C.BHAllyslys₂lys₄lys₈lys₁₆ BRI2999

(2 ml) 가 (2 ml) BHAlyslys₂lys₄lys₈DBL₁₆ (73 mg, 0.01 mmol)
 (5 ml) IRA - 401(OH) , BH
 Alyslys₂lys₄lys₈lys₁₆ (5 ml) , N,N - - N -
 (pH 9.5, 3 ml) 가 3,6 - (234 mg, 0.60 mmol)
 ol) 가 53 2 가 ,
 (Sephadex LH20,) IR 120(Na)
 , 32 3,6 - BHAlyslys₂lys₄lys₈lys₁₆
 (119 mg) . ¹H nmr(D₂O): 1.0 2.0, 3.18, 3.43, 43.1, 7.22, 7.80,
¹³C nmr (D₂O): 27.2, 32.4, 35.3, 43.7, 49.0, 58.5, 63.6, 128.4, 129.1, 131.4, 136.1, 136.6,
 138.6, 139.0, 145.1, 145.6, 178.4, 184.8, 186.7.

7

4 -

PAMAM 4.0BRI2997

4 - (180 mg, 0.5 mmol) PAMAM 4.0(51 mg, 0.01 mmol) (5 m
 l) 가 53 2 가 ,
 (Sephadex LH20,)
 , 4 - PAMAM 4.0
 (60 mg) . ¹H nmr(D₂O): 2.20, 2.60, 3.14, 3.48, 7.23, 7.47, 7.56, 7.77, 7.93(d,J="6Hz)," 8.56(d,
 J="6Hz)." ¹³C nmr (D₂O): 35.8, 40.5, 43.1, 48.4, 53.6, 55.9, 127.6, 128.6, 130.3, 131.9, 132.5, 133.5,
 134.7, 140.5, 142.7, 177.8, 178.0, 185.4.

8

3,5 -

PAMAM 4.0BRI6039

3,5 - (110 mg, 0.32 mmol) PAMAM 4.0(63 mg, 0.012 mmol)
 (3 ml) 가 53 2 가 ,
 (Sephadex G25,) , 2
 4 3,5 - PAMAM 4.0 (110 mg) . ¹H
 nmr(D₂O): 2.53, 3.08, 3.36, 3.66, 7.90, 7.95. ¹³C nmr (D₂O): 34.8, 41.0, 43.1, 48.0, 53.7, 56.2, 124.
 1, 128.6, 143.5, 148.8, 177.6, 185.0.

9

3,6,8 -

PAMAM 4.0BRI2998

3,6,8 - (250 mg, 0.5 mmol) PAMAM 4.0(51 mg, 0.01 mmol),
 N,N - - N - (pH 9.5, 1 ml) (2 ml) 가 53
 2 가 , IR - 120(Na) (Se
 (2 ml) phadex LH20,) 3,6,8 -
 PAMAM 4.0 (102 mg) . ¹H nmr(D₂O): 2.65, 3.02, 3.30, 3.66,
 8.05, 8.42, 8.59, 8.67. ¹³C nmr (D₂O): 33.2, 38.7, 43.2, 43.7, 47.8, 54.0, 54.3, 56.7, 131.0, 131.3, 131.
 9, 135.9, 138.0, 139.6, 143.8, 144.1, 145.6, 176.2, 176.5, 186.0.

3,6,8 - BHAllyslys₂lys₄lys₈lys₁₆ BRI7011
 10
 4 - ()

PAMAM 4.0BRI6040

4 - 4 - () (200 mg, 0.68 mmol) PAMAM 4.0(70 mg, 0.014 mmol)
 DMSO(4 ml) 가 (10⁻⁴ m
 mHg, 40) (1:1) DMSO(5 m
 l) , (130 mg, 1 mmol) (3 ml) 가 4
 , (2 ml) 가 25 mmHg 40
 , 10⁻⁴ mmHg 50 (Sephadex
 G25,) 24 4 - () PAMAM 4.0(24 mg) . ¹H
 nmr(D₂O): 2.25, 2.66, 3.08, 3.20, 3.33, 3.38, 4.01, 7.40(br d), 7.62(br d). ¹³C nmr (D₂O): 36.7, 40.
 9, 43.0, 43.6, 53.5, 55.5, 61.0, 131.6, 135.0, 137.2, 140.4, 174.5, 178.6, 179.2.

11

4 -

PAMAM 4.0(EDA)BRI6116

N - 4 - (100 mg, 0.3 mmol) PAMAM 4.0(EDA)(35 mg, 0.005 m
 mol) 0.1 M pH 8.5 (5 ml) 가 2
 pH 4.5 . 1M (1 ml) 가
 (Sephadex G25,) 32
 4 - PAMAM 4.0(EDA)(47 mg) . ¹H nmr(D₂O): 2.25, 2.42,
 2.63, 3.05, 3.18, 3.31, 3.38, 7.72(d,J="8Hz)," 7.78(d,J="8Hz)." ¹³C nmr (D₂O): 36.0, 40.4, 43.0, 43.7,
 53.7, 55.8, 130.2, 132.2, 140.4, 150.1, 173.6, 178.0, 178.5.

12

N - (4 -)

PAMAM 4.0 (EDA)BRI6117

N - (4 -) (250 mg, 1 mmol) (4 Mℓ) PAMAM 4.0 (EDA)(78 mg, 0.011 mmol) 가 . (Sephadex LH20,) 4 , 64
 N - (4 -) PAMAM 4.0 (EDA)(206 mg) . ¹³ C nmr
¹ H nmr(D₂O): 2.10, 2.48, 2.58, 2.79, 3.2
 0, 7.42(d,J="7Hz)," 7.65(d,J="7Hz)." ¹³ C nmr (D₂O): 36.5, 37.9, 41.1, 53.4, 55.6, 124.8, 130.9, 143.0, 144.2, 177.4, 178.5.

13

4 -

PAMAM 4.0 (EDA)BRI6115

DMSO(3 Mℓ) (195 mg, 1 mmol) DMSO(4 Mℓ) N,N' -
 (530 mg, 2 mmol) 가 20 . DMSO(1 Mℓ)
 PAMAM 4.0 (EDA)(75 mg, 0.011 mmol) 가 18 ,
 (10⁻⁵ mmHg, 35.) DMSO(4 Mℓ) ,
 200 Mℓ 가 . (2)
 (2) , (275 mg) . (Sephadex LH20,)
 32 4 - PAMAM 4.0 (EDA)(106 mg) . ¹ H nmr(D₂
 O): 2.31, 2.55, 2.75, 3.19, 7.32(d,J="9Hz)," 7.63(d,J="9Hz)." ¹³ C nmr (D₂O): 36.3, 40.7, 43.3, 43.8, 53.7, 55.7, 123.3, 130.9, 140.9, 146.0, 161.4, 178.2, 178.6.

14

N,N,N -

BHAlyslys₂lys₄lys₈lys₁₆ BRI2922

(4 Mℓ) (2 Mℓ) BHAlyslys₂lys₄lys₈DBL₁₆ (220 mg, 30 μ mol)
 가 pH 8.5 2 , . DMSO(5 Mℓ)
 (0.50 g, 1.8 mmol) 가 . 4 - N,N,N -
 (50 /10⁻⁵ mmHg) ,
 (3) ,
 (1.128 g) . (Sephadex LH20,) N,N,N -
 BHAlyslys₂lys₄lys₈lys₁₆ (116 mg) . ¹³ C nmr (D₂O): 25.5, 30.5, 3
 0.8, 33.4, 42.1, 56.5, 57.1, 67.5, 68.1, 166.7, 167.0, 167.1, 176.0, 176.2.

15

4 -

PAMAM 4.0BRI6043

1,1' - (85 mg, 0.52 mmol) DMF(4 Mℓ) 4 - (154
 mg, 0.5 mmol) 가 2
 가 DMF(2 Mℓ) PAMAM 4.0(58 mg, 0.011 mmol) 가
 (10⁻⁴ mmHg/30) (Sephadex LH
 20, 10% AcOH) 24 4 - PAMAM 4.0(89 mg)
 .¹H nmr(D₂O): 1.96, 2.65 - 2.85, 3.25 - 3.55, 3.64, 7.92. ¹³C nmr (D₂O): 25.8, 33.1,
 33.5, 38.7, 43.1, 43.5, 53.5, 54.1, 56.4, 61.2, 124.8, 133.6, 139.9, 153.2, 173.2, 176.3, 176.8, 182.6.

6 4 - PAMAM 2.0

16

4 - ()

PAMAM 4.0BRI6044

4 - 4 - () (150 mg, 0.5 mmol) DMSO(3 Mℓ) PAMAM 4.0
 (52 mg, 0.01 mmol) 가 20
 (pH 8.5). (10⁻⁵ mmHg/40)
 (1:1) (2) (2)
 4 - () 25% (20 Mℓ)
 (5 Mℓ) IRA - 401(OH)
 (Sephadex G10, 10% AcOH)
 24 4 - () PAMAM 4.0(90 mg) .¹H nmr(D₂O):
 1.88, 2.65 - 2.80, 2.98, 3.10 - 3.60, 7.52(br d,J="9Hz)," 7.72(br d,J="9Hz)." ¹³C nmr (D₂O): 26.6, 33.4,
 38.8, 43.2, 43.5, 53.6, 53.6, 54.1, 56.8, 62.8, 73.0, 132.1, 135.3, 137.5, 140.0, 176.4, 176.9, 183.6.

17

N - (2 -) - N,N - ()

PAMAM 4.0

1,1' - (85 mg, 0.52 mmol) DMF(3 Mℓ) N - (2 -) - N - (
) - N,N - (135 mg, 0.5 mmol) 가 2
 DMF(2 Mℓ) PAMAM 4.0(60 mg, 0.012 mmol) 가
 2 (10⁻⁴ mmHg/40)
 (Sephadex G10, 10% AcOH) 24 N - (2 -) - N,N - (
) PAMAM 4.0(64 mg) .¹H nmr(D₂O): 1.93, 2.05, 2.70, 3.10 - 3.60, 3.28,
 3.93(m), 4.14, 4.48(m). ¹³C nmr (D₂O): 24.6, 26.2, 33.2, 38.7, 42.8, 42.9, 53.9, 57.4, 62.6, 67.3, 67.5,
 168.9, 176.4, 176.8, 177.3, 183.2.

18

PAMAM 4.0BRI6042

PAMAM 4.0(63 mg, 0.012 mmol) , (5 Mℓ) (170 mg, 0.61 mmol)(pH 10.5)
 80 2 가 , (Sephadex G10, 10%
 AcOH) 24 PAMAM 4.0(107 mg) . ¹H n
 mr(D₂O): 2.00, 2.80(br t), 3.09(br t), 3.32, 3.45(br t), 3.60(br t). ¹³C nmr (D₂O): 25.2, 33.2, 33.4,
 38.7, 41.2, 42.6, 43.4, 44.7, 53.5, 54.0, 56.3, 176.5, 176.7, 176.9, 181.6.

6 PAMAM 2.0

19

4 - ([1,4,8,11 -])

PAMAM 4.0BRI6041

1 - (4 -) - 1,4,8,11 - (120 mg, 0.25 mmol), N -
 (60 mg, 0.52 mmol), 1 - (3 -) - 3 - (250 mg, 1.3 mmol)
 pH 7 (10 Mℓ) 1 , pH 7 (10 Mℓ) PAM
 AM 4.0 (32 mg, 0.006 mmol) 가 . (S
 ephadex LH20, 10% AcOH) 12 4 - ([1,4,8,11 -])
 PAMAM 4.0(80 mg) , ¹H ¹³C nmr ,
 IRA - 401(Cl) (1 Mℓ) , HCl(1 Mℓ)
 가 (30 Mℓ) (68 mg).
¹H ¹³C nmr 가 50% . ¹H nmr(D₂O): 2.17, 2.36, 2.
 50, 2.78, 2.85, 3.25, 3.40, 3.50, 3.60, 3.62, 4.49, 7.63(br d), 7.78(br d). ¹³C nmr(D₂O): 22.7, 23.1, 33.
 2, 38.8, 39.9, 40.2, 40.3, 41.0, 41.2, 42.0, 42.9, 43.2, 43.6, 45.5, 46.1, 49.1, 52.2, 53.9, 54.3, 56.6, 62.7,
 132.5, 135.7, 137.1, 139.7, 174.3, 176.2, 176.2, 176.3, 176.7, 177.0, 178.2, 178.5.

20

4 - - 3 -

PAMAM 4.0(EDA)BRI6119

(32 mg, 0.5 mmol) PAMAM 4.0(EDA)(69 mg, 0.01 mmol), 4 - - 2 -
 (83 mg, 0.5 mmol), (42 mg, 0.5 mmol) (4 Mℓ) 가 .
 4 ,
 (Sephadex LH20,) 32 4 - - 3 - PA
 MAM 4.0(EDA)(91 mg) . ¹H ¹³C nmr(D₂O) 가
¹³C nmr(D₂O): 37.0, 41.1, 50.9, 53.
 4, 55.5, 55.8, 61.5, 120.9, 122.2, 122.4, 132.3, 132.7, 135.0, 135.8, 163.5, 163.7, 169.9, 178.6, 179.3. ¹
 H nmr (D₂O): 2.20, 2.35, 2.60, 3.15, 3.30, 3.55, 4.25, 6.68, 7.12, 7.55.

21

4 -

PAMAM 4.0(EDA)

4 - mmol) 가 . (86 mg, 0.48 mmol) (20 Mℓ) NaHCO₃ PAMAM 4.0(EDA) (69 mg, 0.01 mmol) (24) (68 mg) (S)

22

3,5 - PAMAM 4.0(EDA) (112 mg, 0.5 mmol) (5 Mℓ) PAMAM 4.0(EDA) (70 mg, 0.01 mmol) (24) (112 mg) (S)

23

4 - - PAMAM 4.0(EDA) (251 mg) (2 Mℓ) PAMAM 4.0(EDA) (69 mg, 0.01 mmol) (24) (86 mg) (S)

24

4 - () PAMAM 4.0(EDA) (97 mg) (30 Mℓ) PAMAM 4.0(EDA) (69 mg, 0.01 mmol) (24) (102 mg) (S)

25

4 - - () PAMAM 4.0(EDA) (109 mg) DMF (30 Mℓ) PAMAM 4.0(EDA) (69 mg, 0.01 mmol) (24) (30 mg) (S)

Cn_n - 2 -
 [(8 - N -) 5 - -4,7,8,9 - -O - -3,5 -
 2 - -D - -D - -2 -]

(1 Mℓ) 5 - -4,7,8,9 - -O - -2 - S - -3,5 -
 -2 - -D - -D - -2 - (Hasegawa , 1986)(100 mg) 8 -
 (41 mg) (280 mg) 가 17 20
 5%
 (26 mg) (130 mg) (5 Mℓ) , N -
 (46 mg) 가 20 17
 (97 mg, 71%)

[(11 - N -) 5 - -4,7,8,9 - -O - -3,5 -
 -2 - -D - -D - -2 -]

[(- N -) 5 - -4,7,8,9 - -O - -3,5 - -2
 - -D - -D - -2 -]

[(4 - N -) 5 - -4,7,8,9 - -O - -3,5 -
 2 - -D - -D - -2 -]

[(4 - N -) 5 - -4,7,8,9 - -O - -3,5 -
 -2 - -D - -D - -2 -]

APAMAM [EDA] 4.0 [(8 -) -5 - -3,5 - -2 - -D - -D -
 2 -]₃₂ BRI 6112

(4 Mℓ) PAMAM [EDA] 4.0(50 mg) [(8 - N -
) 5 - -4,7,8,9 - -O - -3,5 - -2 - -D - -
 -D - -2 -] (300 mg) 가 20 60
 (2 Mℓ) Sephadex LH20
 PAMAM [EDA] 4.0 [[(8 -)
 5 - -4,7,8,9 - -O - -3,5 - -2 - -D - -D - -2 -
]]₃₂ (182 mg, 93%)

20 (3 Mℓ) PAMAM [EDA] 4.0 [(8-) 5- -4,7,8,
 9- -O- -3,5- -2- -D- -D- -2-]]₃₂ (1
 82 mg) , 0.19 M (7 Mℓ) 가 , 2.5
 phadex LH20 (10 Mℓ) , 3 Se
) -5- -3,5- -2- -D- -D- -2-]
 (110 mg, 77%) .

PAMAM [EDA] 4.0 [(11-) -5- -3,5- -2- -D- -D-
 -2-]₃₂ BRI 6147

PAMAM [EDA] 4.0 [() -5- -3,5- -2- -D- -D- -2-
]₃₂ BRI 6121

PAMAM [EDA] 4.0 [(4-) -5- -3,5- -2- -D- -D-
 -2-]₃₂ BRI 6120

BBHA lyslys₂lys₄lys₈lys₁₆ [(8-) -5- -3,5- -2- -D- -D-
 -2-]₃₂ BRI 6169

(2 Mℓ) (2 Mℓ) BHA lyslys₂lys₄lys₈lys₁₆ (t - Boc)₃₂ (20.3 mg)
 20 2 (25 mg) , [(8- N-) 5- -4,7,8,9-
 -O- -3,5- -2- -D- -D- -2-]](78 mg)
 가 . 20 60 ,
 0.1M (2.5 Mℓ) , 20 3
 (1 Mℓ) , 17
 Sephadex LH20 BHA lyslys₂lys₄lys₈lys₁₆
 [(8-) -5- -3,5- -2- -D- -D- -2-
]₃₂ (44 mg, 86%) .

27

4-

4- -5- -7,8,9- -O- -2-S- -3,4,5- -2-
 -D- -D- -2- (150 Mℓ) 4-
 -5- -7,8,9- -O- -2- -3,4,5- -D- -D- -2-
 20 (Sabesan, 1994) (5 g) (5.8 g) 가
 48 (5.2 g)
 HPLC[C₁₈ , 30% /] (3.9 g, 72%)
 [(8- N-) 4- -5- -7,8,9- -O- -3,4,5-
 -2- -D- -D- -2-]

5 - (3.5 Mℓ) 4 - - 5 - - 7,8,9 - - O - - 2 - S - - 3,4,
 55 mg) - 2 - - D - - D - - 2 - (300 mg) 8 - (1
 (1.26 Mℓ) 가 20 17 .
 10% .
 (95 mg) (385 mg) 가 (20 Mℓ) , N -
 (175 mg) 20 17
 HPLC[C₁₈ , 30% /]
 (340 mg, 83%) .

APAMAM [EDA] 4.0 [(8 -) - 4 - - 5 - - 3,4,5 - - 2 - - D - -
 - D - - 2 -]₃₂ BRI 6146
 (5 Mℓ) PAMAM [EDA] 4.0(72 mg) [(8 - N -
) 4 - - 5 - - 7,8,9 - - O - - 3,4,5 - - 2 - - D -
 - D - - 2 -] (318 mg) 가 20 60
 (2 Mℓ) . Sephadex
 x LH20 PAMAM [EDA] 4.0 [[(8
 -) 4 - - 5 - - 7,8,9 - - O - - 3,4,5 - - 2 - - D - -
 - D - - 2 -]]₃₂ (225 mg, 81%) .

20 (1 Mℓ) PAMAM [EDA] 4.0 [[(8 -) 4 - - 5 -
 - 7,8,9 - - O - - 3,4,5 - - 2 - - D - - - D - - 2 -]
]₃₂ (215 mg) , 1M (1 Mℓ) 가 , 3
 (2 Mℓ) , 17 .
 Sephadex LH20 PAMAM [EDA] 4.0 [(
 8 -) 4 - - 5 - - 3,4,5 - - 2 - - D - - - D - - 2 -
]₃₂ (160 mg, 90%) .

BPAMAM [EDA] 4.0 [(8 -) - 4 - - 5 - - 3,4,5 - - 2 - - D - -
 - D - - 2 -]₃₂ BRI 6149
 20 5 , (40 Mℓ) (20 Mℓ) PAMAM [EDA] 4.0 [(8 -) - 4 - - 5 -
 - 3,4,5 - - 2 - - D - - - D - - 2 -]₃₂ (25 mg)
 , (5 Mℓ) , 0.45 μm .
 - D - , PAMAM [EDA] 4.0 [(8 -) - 4 - - 5 - - 3,4,5 - - 2 -
 - D - - D - - 2 -]₃₂ (23 mg, 96%) .

28

4 - N -
 (5 Mℓ) 4 - (500 mg) N - (380 mg)
 (680 mg) 가 20 64 ,
 (100 Mℓ) .

(730 mg, 92%)

PAMAM [EDA] 4.0 [4 -

] ₃₂ BRI 6160

N - (5 Mℓ) PAMAM [EDA] 4.0 (69 mg) 4 -
 (130 mg) 가 20 65 가
 1M (1 Mℓ) 가 24
 10% (5 Mℓ) 10% Sephadex LH
 20 PAMAM [EDA] 4.0 [4 -
]₃₂ (110 mg, 94%)

29

3,6 -

BHAlyslys₂lys₄lys₈lys₁₆lys₃₂

(2 Mℓ) (2 Mℓ) BHAlyslys₂lys₄lys₈lys₁₆ DBL₃₂ (147 mg)
 가 2 N,N - - N -
 (pH 9.5, 5 Mℓ) , 3,6 - (400 mg) 가
 1M 가 pH 9.5 53 3 가
 IR 120(Na)
 (Sephadex LH20,) 64 3,6 -
 BHAlyslys₂lys₄lys₈lys₁₆lys₃₂ (175 mg)

30

3,5 -

BHAlyslys₂lys₄lys₈lys₁₆lys₃₂

(3 Mℓ) (3 Mℓ) BHAlyslys₂lys₄lys₈lys₁₆ DBL₃₂ (300 mg, 0.02 mm
 ol) 가 2 (187 mg)
 , IRA 401(OH) (8 Mℓ) , 3,5 - (680 mg, 2 mm
 ol) 가 / 1:1 가 53 3 가 ,
 (Sephadex LH20,) 64 3,6 -
 BHAlyslys₂lys₄lys₈lys₁₆lys₃₂

31

3,5 -

BHAlyslys₂lys₄lys₈lys₁₆lys₃₂ BRI 6741

ol) (3 Mℓ) (3 Mℓ) BHAlyslys₂lys₄lys₈lys₁₆ DBL₃₂ (300 mg, 0.02 mm
 가 2
 , IRA 401(OH) (186 mg)
 / 1:1 (8 Mℓ) , 3,5 - (450 mg,
 2 mmol) 가 . 53 13 가 ,
 . (Sephadex LH20,) 64 3,6 -
 BHAlyslys₂lys₄lys₈lys₁₆lys₃₂
 3,5 - PAMAM 4.0 (EDA)BRI 6195
 32
 4 -

BHAlyslys₂lys₄lys₈lys₁₆lys₃₂ BRI 6181

ol) (2 Mℓ) (2 Mℓ) BHAlyslys₂lys₄lys₈lys₁₆ DBL₃₂ (147 mg, 0.01 mm
 가 2
 N,N - - N - (pH 9.5, 5 Mℓ) , 4 -
 (250 mg) 가 . 1M pH 10 , 53
 3 가 ,
 IR 120(Na) (Sephadex LH20,)
 64 4 - BHAlyslys₂lys₄lys₈lys₁₆lys₃₂ (150 mg)
 .
 33
 4 -

BHAlyslys₂lys₄lys₈lys₁₆lys₃₂

ol) (2 Mℓ) (2 Mℓ) BHAlyslys₂lys₄lys₈lys₁₆ DBL₃₂ (147 mg, 0.01 mm
 가 2
 N,N - - N - (pH 9.5, 5 Mℓ) , 4 - (250
 mg) 가 . pH 9 , 53 3
 가 ,
 IR 120(Na) (Sephadex LH20,) 64
 4 - BHAlyslys₂lys₄lys₈lys₁₆lys₃₂ BRI 6196 ,
 (152 mg) .
 34
 4,6 -

PAMAM 4.0

(2 Mℓ) 4,6 - (165 mg) (2 Mℓ) PAMAM 4.0(5
 1 mg, 0.01 mmol) 가 . pH 9.5 , 1
 , 53 3 가 ,

6 - (Sephadex G25,) 24 4,
PAMAM 4.0(81 mg) , .

35

PAMAM 4.0 (EDA)

(3 Mℓ) PAMAM 4.0 EDA(74 mg, 0.01 mmol) (188 mg)
가 . 가 pH 9 ,
(Sephadex LH20,) 21
PAMAM 4.0 (EDA)(193 mg) , .

36

(- 3 -) -

PAMAM 4.0 (EDA)

(5 Mℓ) PAMAM 4.0 (EDA)(69 mg, 0.01 mmol) (- 3 -) (100 mg,
0.5 mmol) 가 . 1M 가 (pH 10). ,
53 2 가 , ,
(Sephadex LH20,) 32 (- 3 -) PAMAM 4.0 (ED
A) , (87 mg) .

37

PAMAM 2.0 .BRI - 6807

PAMAM 2.0 (0.0479 mmol, 50 mg) MeOH 0.5 Mℓ , 10 Mℓ
1 - N - 12 - (0.14 g, 0.384 mmol), N -
[HOBT](52 mg, 0.384 mmol), (53 μℓ, 0.384 mmol) 1 - (3 - - 3 -)
HCl[EDC](74 mg, 0.384 mmol) 가 .
1/3 , LH20
PAMAM 2.0

¹H nmr(D₂O): 1.15, 1.45, 1.9, 2.15, 2.75, 2.8, 3.15, 3.35, 3.5, 4.55, 8.05, 8.5, 8.8.

PAMAM 4.0 BRI - 6809

PAMAM 4.0 (0.05 mmol, 69 mg) MeOH 1.0 Mℓ , 15 Mℓ
 1 - N 12 - (0.143 g, 0.4 mmol), N - [HOBT]
 (77 mg, 0.4 mmol), (56 μℓ, 0.4 mmol) 1 - (3 -) HC
 I[EDC](77 mg, 0.4 mmol) 가 .

LH20 1/3 , 1%
 PAMAM 4.0 NH₂ 가 .

¹H nmr(D₂O): 1.10, 1.45, 1.9, 2.1, 2.30, 2.5, 2.7, 3.2, 4.5, 8.00, 8.45, 8.80.

38

PAMAM 4.0 BRI - 6157
 (25 Mℓ) PAMAM 4.0 (275 mg, 39.8 μ M) 6 - (
) (400 mg, 1.67 mM) 가 24
 pH 10 10.5 24
 , Sephadex LH20
 , (450 mg, 78%)
 .

¹H nmr(D₂O): 2.20, 2.50, 3.23, 3.46, 3.63, 7.52 7.87.

BHA.Lys.Lys₂.Lys₄.Lys₈.Lys₁₆.Lys₃₂ .. BRI - 6189 .

39

(Venom)

A

(microphysiometer)(Molecular Deviecs Inc.) (Pa

rce , 1989; McConnell , 1992).

CEM - - / - RPMI 1640 (Molecular Deviecs Inc.
 , , ") (Molecular Deviecs)
 (3 μm) 60,000 75,000 가 (Molecu
 lar Deviecs Inc.) pH ()
 8 . 100 120 μℓ/ 가 .

(CO₂)
 , 30 , (가 4 5)
 (μV/s) (가 4 5)
 37 . 2
 () 30 , / 4 가
 BRI2923 , 1 가
 BRI 2923 , pH 7.2 , 100 μM 1 nM / 가
 , 6 (가) 1 , .
 3
 B
 BRI2923
 (Naja malenoleuca) . CEM 가
 가 , () 80%
 가 , 10 100% 10, 50 100 μg/
 Mℓ . 50 μg/Mℓ . BRI2923 가
 (10⁻⁴ M 10⁻⁵ M)
 가 80% (6 , 30 60) , 50 μg/Mℓ 10⁻⁵ M BRI2923
 5% , 15 20
 50 μg/Mℓ 10⁻⁴ M BRI2923 , 가
 . 100 μg/Mℓ 10⁻⁴ M BRI2923 가 ,
 /
 (melittin)
 .Naja malenoleuca 가 ()
 , 가 (, BRI2923)
 6 30 60
 () BRI2923
 10⁻⁵ M 10⁻⁷ M ½log CEM 가 . (10⁻⁵ M
 5 x 10⁻⁶ M) 15 . 10⁻⁶ M
 가 , 1 , . 5 x 10⁻⁷ M
 , 10⁻⁷ M . 10⁻⁶ M BRI2923
 BRI2923 10⁻⁶ M 20 . 10⁻⁴ M
 10⁻⁵ M BRI2923 . 10⁻⁶ M BRI2923 30
 , 30 , 10 15% . BRI
 2923 10⁻⁷ M, 5 x 10⁻⁷ M 10⁻⁸ M . 10⁻⁹ M BRI2923 10⁻
 6 M

HIV(AIDS)

Vpr (HIV - 1) 14 - kDa, 96 vpr
 HIV - 1, HIV - 2, Vpr HIV (Cullen, 1998, E
 merman & Malim, 1998). Vpr
 (Stewart, 1997; Zhao, 1996; Macreadie, 1996).

Vpr Vpr P3 Vpr P3 CD
 4+ T (CEM) P3 (Arunagiri, 1997).

CEM 1400 RPM 7 RPMI 1640
 가 (spotting) Molecular Deviecs Inc. 43,000 75,000
 120 μ l 가
 30 60
 30
 (μ V/s) 가 4
 5 4
 37

CEM log 1.3×10^{-5} 1.3×10^{-6} /Ml
 Vpr P3 30
 Vpr P3 10^{-5} M 2×10^{-5} M Vpr P3
 2

BRI2923 Vpr Vpr P3
 , BRI2923 가 , 20 30
 , BRI2923 Vpr P3 Vpr P3
 Vpr P3 Vpr P3/BRI2923 2 30
 4) (

M Vpr P3 가 , CE

1 (RPMI) 30 , Vpr P3 (10^{-5} M) 10^{-4} M () BRI2923 1 M (25 M) , 10^{-4} M BRI2923 () () pH BRI2923 , BRI2923 , (a) 1 가 , (b)

2 10^{-4} M BRI2923 10^{-5} M Vpr P3 () 4 . 3 4 10^{-5} M BRI2923 2×10^{-5} M Vpr P3 (3) . BRI2923 10^{-6} M 2×10^{-5} M Vpr P3 (3) . 2×10^{-5} M Vpr P3 10 (2) . , BRI2923 가 Vpr P3 . BRI2923

41

· HPC - 8

, AM

· # C - 1430

· $C_{46}H_{46}N_2O_{23}$, 994.87

· 10 mM , 100 μ l (DMSO) 1 mg .

· (Sigma Cat. No. C8052) - 5 B A

· - BRI2913 BRI2999

1. 2 PBS() , log HCP - 8() 2 Ml/75 cm² (EDTA) .

2. 5
3. 20 Mℓ 가
4. 50 Mℓ (RT) 7 1200 RPM
5. PBS , RT 7 1200 RPM
6. PBS , , RT 7 1200 RPM ,
7. 5 μℓ PBS 1 Mℓ 가 , 37 45
8. PBS(5 20 Mℓ) , PBS 5 x 10⁵ /100 μℓ
9. (H₂O) 50 μℓ (DMSO 10 mM PBS)
50 μℓ 96 100 μℓ (5 x 10⁵ /) 가 3
10. 5% CO₂ 37 2
- 12.

3

	(FI)	(%)
0.3 mg/Mℓ 100 μ M BRI2923 100 μ M BRI2999	72.16659.5	0%8.5%17.5%
0.15 mg/Mℓ 100 μ M BRI2923 100 μ M BRI2999	65.86159.4	0%7.3%9.7%
(SR)	26.8	
% = "100" - (FI + /FI x 100)		

Arunagiri, C.K., Macreadie, I.G., Hewish, D.R. and Azad, A.A. (1997) A C-terminal domain of HIV-1 accessory protein Vpr is involved in penetration, mitochondrial dysfunction and apoptosis of human CD4⁺ lymphocytes. *Apoptosis*, **2**, 69-76

Cullen, B.R. (1998) HIV-1 auxiliary proteins: making connections in dying cells. *Cell*, **93**, 685-692.

Emerman, M., and Malim, M.H. (1998) HIV-1 regulatory/accessory genes: keys to unravelling viral and host cell biology. *Science*, **280**, 1880-1883.

McConnell, H.K., Owicki, J.C., Parce, J.W., Miller, D.L., Baxter, G.T., Wada, H.G. and Pitchford, S. (1992). The cytosensor microphysiometer: biological applications of silicon technology. *Science*, **257**, 1901-1912.

Macreadie, I.G., Arunagiri, C.K., Hewish, D.R., White, J.F., and Azad, A.A. (1996) Extracellular addition of a domain of HIV-1 Vpr containing the aminoacid sequence motif H(S/F)RIG causes cell membrane permeabilization and death. *Mol. Microbiol.*, **19**(6), 1185-1192.

Parce, J.W., Owicki, J.C., Kercso, K.M., Sigal, G.B., Wada, H.G., Muir, V.C., Bousse, L.J., Ross, K.L., Sikic, B.I. and McConnell, H.M. (1989). Detection of cell-affecting agents with a silicon biosensor. *Science*, **246**, 243-247.

Stewart, S.A., Poon, B., Jowett, J.B.M. and Chen, I.S. (1997) Human immunodeficiency virus type 1 Vpr induces apoptosis following cell cycle arrest. *J.Virol*, **71**, 5579-5592.

Zhao, Y., Cao, J., O'Gorman, M.R.G., Yu, M., and Yogeve, R. (1996) Effect of human immunodeficiency virus type 1 protein R (Vpr) gene expression on basic cellular function of fission yeast *Schizosaccharomyces pombe*. *J.Virol*, **70**, 5821-5826.

(57)

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2.

1 , 2 가 , 2

3.

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2 ,

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2 ,

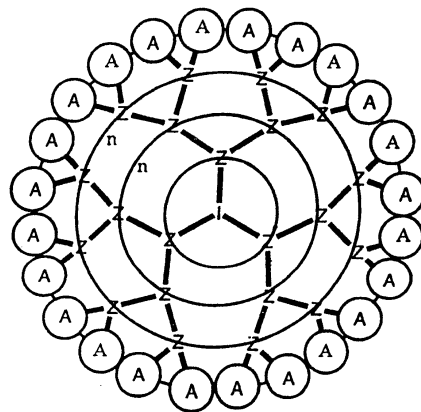
6.

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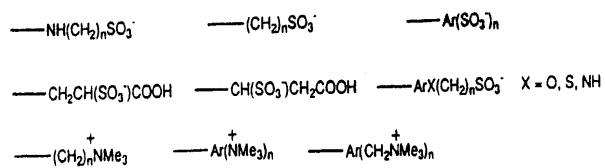
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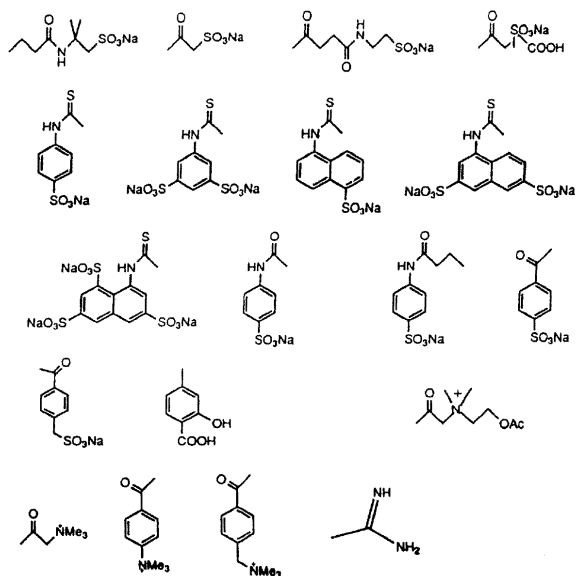
9.

1 8 () , 1 , 2 , 3
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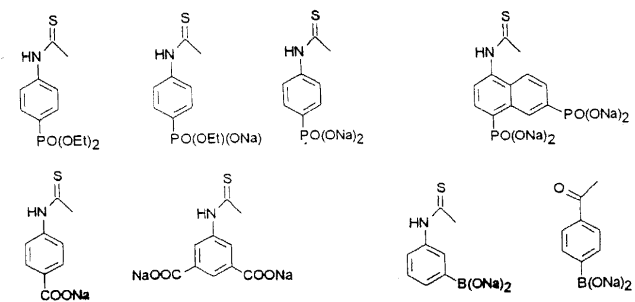
10.

1 9 () n 0 :





—ArXP(=O)(OR)₂ X=O, CH₂, CHF, CF₂ R=알킬, 아릴, H, Na
 —ArXP(=O)(OR¹)(NR²R³) X=O, CH₂, CHF, CF₂ R¹=알킬, 아릴, H, Na R², R³=알킬, 아릴
 —Ar[P(=O)(OR)₂]_n R=알킬, 아릴, H, Na n=1-3
 —Ar[B(OH)₂]_n n=1-3 —Ar[COOH]_n n=1-3



- 9. 3,6,8 - - ,
- 10. 4 - () ,
- 11. 4 - ,
- 12. N - (4 -) ,
- 13. 4 - ,
- 14. N,N,N - - ,
- 15. 4 - ,
- 16. 4 - () ,
- 17. N - (2 -) - N,N - () - ,
- 18. ,
- 19. 4 - ([1,4,8,11 -]) ,
- 20. 4 - - 3 - - ,
- 21. 4 - ,
- 22. 3,5 - ,
- 23. 4 - ,
- 24. 4 - () ,
- 25. - 4 - () ,
- 26. (8 -) - 5 - - 3,5 - - 2 - - D - - - D - - 2 - ,
- 27. (11 -) - 5 - - 3,5 - - 2 - - D - - - D - - 2 - ,
- 28. () - 5 - - 3,5 - - 2 - - D - - - D - - 2 - ,
- 29. (4 -) - 5 - - 3,5 - - 2 - - D - - - D - - 2 - ,
- 30. (4 -) - 5 - - 3,5 - - 2 - - D - - - D - - 2 - ,
- 31. (8 -) - 4 - - 5 - - 3,4,5 - - 2 - - D - - - D - - 2 - ,

32. (8 -) - 4 - - 5 - - 3,4,5 - - 2 - - D - - - D - - 2 -

33. 4 - ,

34. 3,5 - ,

35. 4 - ,

36. 4 - ,

37. 4,6 - ,

38. ,

39. (- 3 -) - ,

40. ,

41. .

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13.

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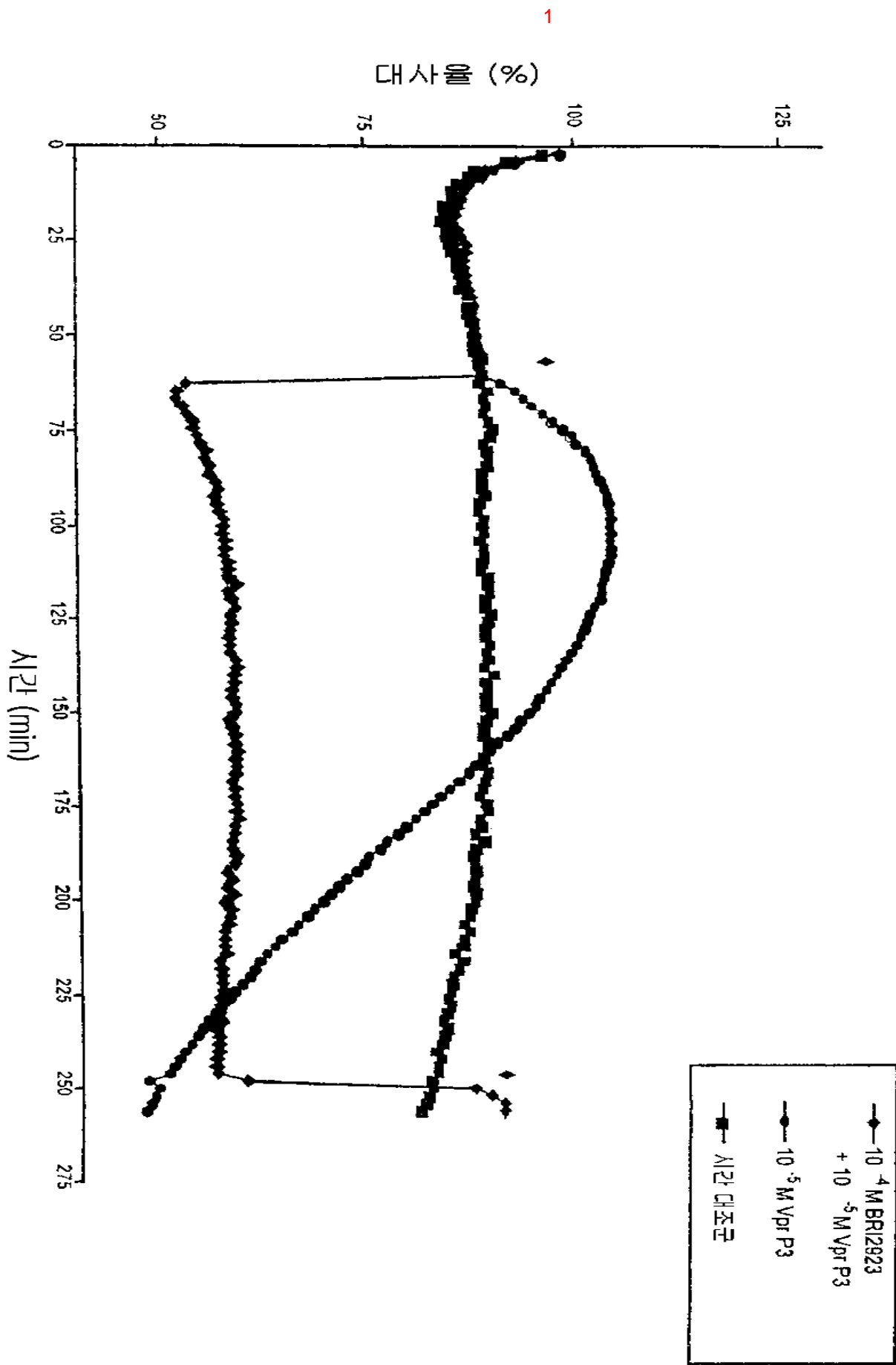
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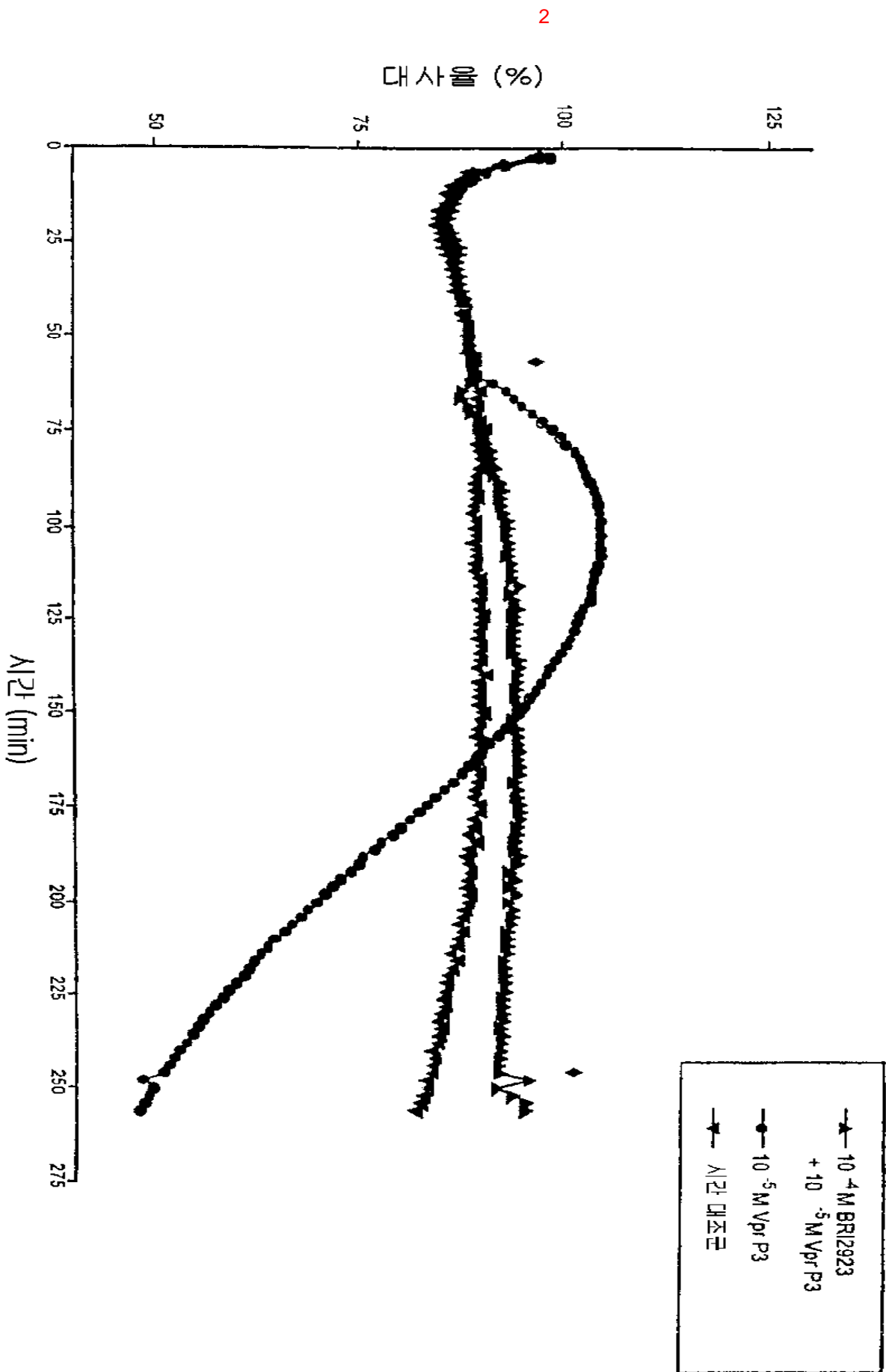
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10e-5M Vpr P3의 10e-4M BR12923 억제
(보정하지 않음)

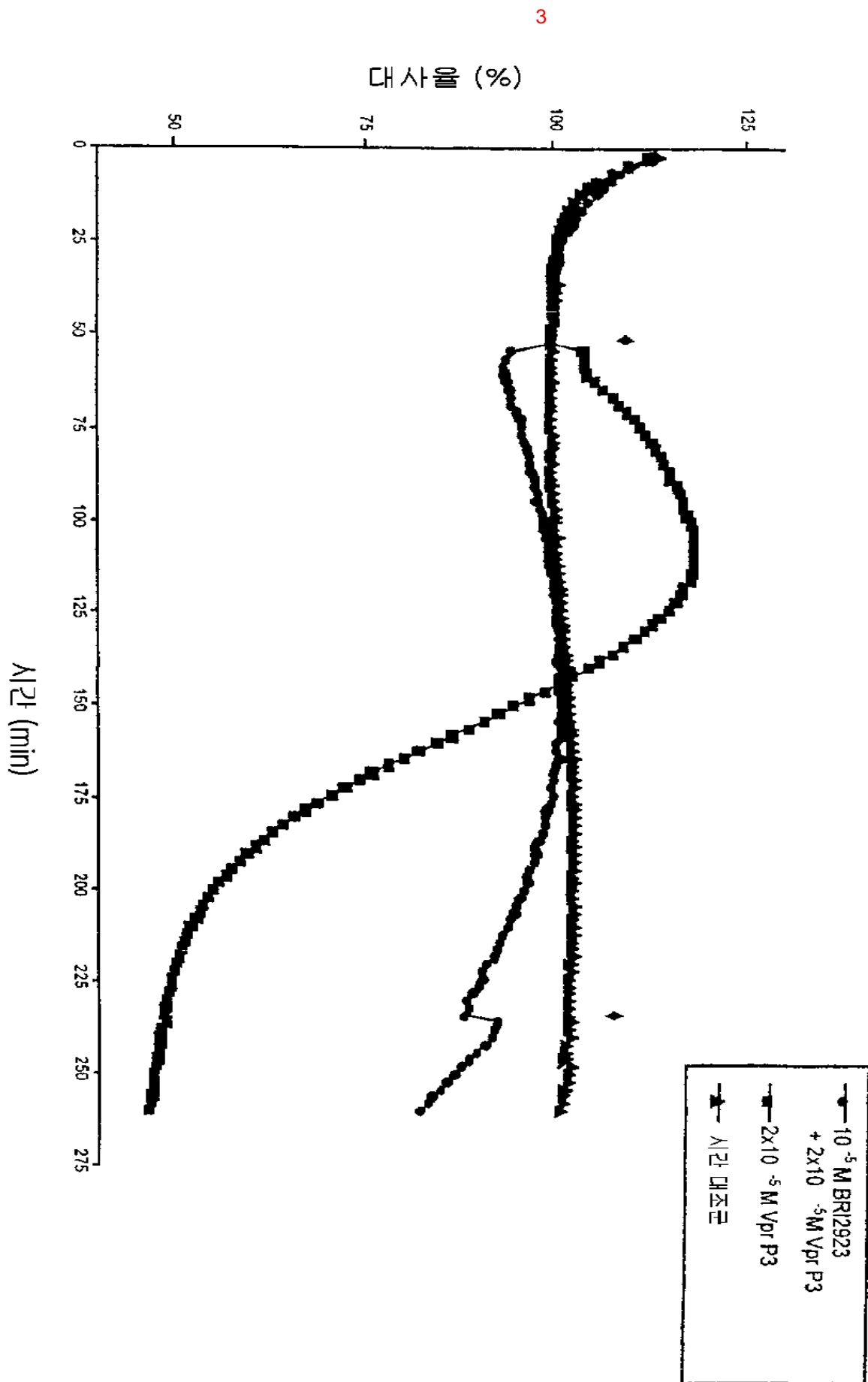


10e-5M Vpr P3의 10e-4M BR12923 억제
(보정함)



2x10⁻⁵M Vpr P3의 10⁻⁵M BRI2923 억제

(보정하지 않음)



4

2x10⁻⁵M Vpr P3의 10e-5M & 10e-7M BRI2923 억제
(보정하지 않음)

